TRANSMITTAL LETTER

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In re Application of:
MEULMAN, DIRK et al.

Serial No.: 09/380,695

Filing Date: March 29, 2002

For: USE OF A 7α-METHYL-17α-ETHYNYL-ESTRANE DERIVATIVE FOR THE TREATMENT OF ATHEROSCLEROSIS

Docket: 1997.263 US

Examiner: Wang, S.

Group Art Unit: 1617

CERTIFICATE OF FACSIMILE TRANSMISSION
I hereby certify that this BRIEF ON APPEAL (14 sheets) is being telefaxed to facsimile machine 571-273-8300 in the United States Patent and Trademark Office on this 7th day of December, 2005 by the undersigned.

Lynn Brush

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

☒ Transmitted herewith find the document(s) related to this application:

1. **TRANSMITTAL LETTER IN DUPLICATE;**
2. **APPEAL BRIEF; and;**
3. **CERTIFICATE OF FACSIMILE**

☒ Applicant hereby petitions for an extension of time under 37 CFR 1.136 of:

☐ One Month	($ 120.00)	☐ Two Months	($ 450.00)
☐ Three Months	($1020.00)	☒ **Four Months**	**($1590.00)**
☒ **Appeal Brief**	**($ 500.00)**		

The total fee believed due is **$2090.00.** Please charge this amount and any other fees which may be due (including filing fees under 37 CFR 1.16 and processing fees under 37 CFR 1.17) to Deposit Account No. 01-1350. If an extension of time is required but has not been requested above, Applicant hereby petitions for an extension of time sufficient for the attached document(s) to be timely. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

David H. Vickrey
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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BRIEF ON APPEAL

Respectfully submitted,

David H. Vickrey
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Dated: December 7, 2005

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APPEAL BRIEF

INTRODUCTION

Appellants respectfully submit this Appeal Brief pursuant to 37 C.F.R. § 41.37 in support of their appeal in this application, which has been finally rejected. The Appellants filed a Notice of Appeal on June 8, 2005. The fee under 37 C.F.R. § 41.37 and § 41.20(b)(2) is provided below.

REAL PARTY IN INTEREST

The real party in interest is the assignee of record Akzo Nobel N.V. at P.O. Box 9300, Nl-6800 SB, Arnhem, The Netherlands. Akzo Nobel N.V. is the assignee of the entire right, title and interest in the present application.

RELATED APPEALS AND INTERFERENCES

There are no other prior or pending appeals, interferences or judicial proceedings known by the undersigned, or believed by the undersigned to be known to Appellants or the assignee, "which may relate to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal."

STATUS OF CLAIMS

Claims 1-4, and 6 are pending and have been rejected. All of the pending claims, Claims 1-4, and 6 are being appealed.

Claim 5 has been cancelled.

STATUS OF AMENDMENTS

No amendment has been submitted subsequent to the Office Action of December 14, 2004.

SUMMARY OF CLAIMED SUBJECT MATTER

The claimed subject matter of the present invention relates to a method of inhibiting the atherosclerotic process. In Claim 1 the method of inhibiting the atherosclerotic process involves administering to a mammal an effective amount of a 7α-methyl-17α-ethynyl-estrane derivative of a certain general formula. Claims 2 and 3, dependent on Claim 1, further define the formula. Claim 4, also dependent on Claim 1, claims the employment of 7α-methyl-17α-ethynyl-17β-hydroxy-estra-5(10)-en-3-one as the 7α-methyl-17α-ethynyl-estrane derivative in the method of Claim 1. In Claim 6, also dependent on Claim1, the mammal is human.

For the purposes of this appeal, all pending claims stand or fall together.

The claimed method of inhibiting the atherosclerotic process is disclosed in the specification, *inter alia*, from Page 4, line 1 to Page 6, line 15 for all claims on appeal.

GROUNDS OF REJECTION TO BE REVIEWED

I. Whether claims 1-4, and 6, which stand rejected under 35 U.S.C. §103(a), are patentable over Haenggi et al.

The Examiner has rejected claims 1-4, and 6 directed to a method for inhibiting the atherosclerotic process by treating a mammel with an effective amount of 7α-methyl-17α-ethynyl-estrane derivative of a certain general formula. According to the Examiner the claimed subject matter is obvious over Haenggi et al. The Examiner states that Haeggi et al. discloses treatment of postmenopausal women with tibolone with a daily amount of 2.4 mg. The Examiner asserts that it is well understood that postmenopausal women suffer from atherosclerosis. On this basis, the Examiner states that it would be prima facie obvious to treat postmenopausal women because there is no obvious reason for NOT using hormone replacement therapy in postmenopausal women suffering from atherosclerosis.

II. Whether claims 1-4, and 6, which stand rejected under 35 U.S.C. §103(a), are patentable over Haenggi et al. in view of in view of Berglund.

The Examiner has also rejected claims 1-4, and 6 as obvious over Haenggi et al. in view of Berglund. The Examiner asserts that Haenggi et al. teaches a method of decreasing lipoprotein by administering tibolone to a human and that Haenggi further teaches that Lp(a) is a strong independent risk factor for coronary disease. The Examiner also asserts that Berglund

discloses Lp(a) has been implicated with the increased risk of atherosclerosis. According to the Examiner it would have been prima facie obvious to employ tibolone as a method of inhibiting atherosclerosis since Lp(a) had been indicated to increase risk of atherosclerosis, tibilone lowers the level of lipoprotein and lowering the level of lipoprotein (a) would have reasonably expected tto inhibit the progress of atherosclerosis. For these reasons the Examiner asserted that the method of inhibiting the atherosclerotic process as claimed is obvious.

ARGUMENT

I. Claims 1-4, and 6 Directed to a a Method for Inhibiting a the atherosclerotic process by treating a mammel with an effective amount of 7α-methyl-17α-ethynyl-estrane derivative of a certain general formula are Non-Obvious Because There is No Teaching or Suggestion to do so in Haenggi et al.

Claims 1-4, and 6 are under final rejection under 35 U.S.C. 103(a) as being unpatentable over Haenggi et al. The Examiner rejected all of the pending claims in the Office Action of December 14, 2004 as obvious under 35 U.S.C. 103(a) over the above-cited reference. According to the Examiner, Haeggni et al discloses treatment of postmenopausal women with tibolone as hormone replacement therapy. The Examiner acknowledges that Haenggi et al. do not expressly teach that the postmenopausal women studied are suffering from atherosclerosis. However, the Examiner states that "a substantial portion of the population of post menopausal women are suffering atherosclerosis", then concludes that there is no obvious reason for NOT (emphasis supplied here) using hormone replacement therapy in postmenopausal women suffering from athersclerosis. *See*, Office Action of December 14, 2004, page 2.

By the Examiner's own statement above, it is clear that the Examiner has engaged in a hindsight analysis. The Examiner's analysis improperly assumes that the method of the current invention should be used to postmenopausal women suffering from athersclerosis, then asks the question whether there is any reason NOT to do so. A more appropriate question is whether there is a teaching or suggestion in Haenggi et al. to use the particular method claimed in the current application to treat those suffering from athersclerosis. As the Appellants make clear below, there is no such teaching or suggestion.

In their April 15, 2004 response to the Office Action, Appellants submitted that tibolone has been the subject of studies assessing its long-term effects on lipid metabolism, since the

compound has, *inter alia*, progestogenic activity as well as androgenic properties, the latter properties are associated with negative effects on lipoproteins, that is causing " a significant decrease in HDL-cholesterol and its major apolipoprotein A-1" (first paragraph of the Discussion on page 648 of Haenggi et al.). However, as Haenggi et al. clearly states in the right column of page 649, the studies indicated that the possibly benefcial effect of tibolone on reducing lipoprotein A serum levels "might counterbalance, at least to some extent, the theoretical adverse effect on the other lipoprotein risk factors, such as the important decrease of high density lipoprotein-cholestrerol and the significant increase in apolipoprotein B."

In this regard, Appellants point out that when evaluating obviousness, one must look at what the references fairly teach. It is impermissible to choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary for a full appreciation of what such reference fairly suggests to one skilled in the art. Instead, the reference must be considered in its entirety. *Bausch & Lomb, Inc. v. Baines-Hind/Hydrocurve, Inc.*, 796 F.2d. 443, 448-449, 230 USPQ 416, 420 (Fed. Cir. 1986).

As noted above, when considered in its entirety, Haenggi et al.disclose both positive and negative effects of tibolone on lipoprotein risk factors. Thus, it can be concluded that Haenggi et al. merely teach that with the administration of tibolone, there is a possible balancing of positive and negative effects on coronary heart disease risk factors. Haenggi et al., when considered in its entirety, does not teach or suggest the unexpectedly strong atheroprotective properties of tibolone.

The non-obvious effects of the currently claimed invention are further exemplified by the data provided in the current application at Table III. There tibolone prevented cholesterol accumulation (expressed as cholesterol level) in the aortic arch while estradiol (decanoate) did not lead to a reduction in cholesterol accumulation. Furthermore, fatty streak formation in the aortic arch was completely prevented by treatment with tibolone, whereas estradiol (decanoate) had only minor effects.

II. Claims 1-4, and 6 Directed to a a Method for Inhibiting a the atherosclerotic process by treating a mammel with an effective amount of 7α-methyl-17α-ethynyl-estrane derivative of a certain general formula are Non-Obvious Because There is No Teaching or Suggestion to do so in Haenggi et al. in view of Berglund

Claims 1-4, and 6 are under final rejection under 35 U.S.C. 103(a) as being unpatentable over Haenggi et al in view of Berglund. The Examiner rejected all of the pending claims in the Office Action of December 14, 2004 as obvious under 35 U.S.C. 103(a) over the above-cited references.

As acknowledged in the Office Action of December 14, 2005 at page 4, Haenggi et al. doe not teach the employment of tibolone in a method of inhibiting atherolsclerosis. Berglund is cited for teaching that lipoprotein (a) has been implicated with an increased risk of atherosclerosis. The Office Action on this basis concludes that it would be prima facie obvious to employ tibolone in a method of inhibiting atherosclerosis. Appellents strongly traverse this conclusion.

As discussed in detail in I. above, the Examiner has inappropriately cited isolated portions of Haenggi et al. for a teaching that tibolone decreases lipoprotein (a), rather than appropriately viewing the reference in its entirety. When this is done, Haenggi et al. in its entirety teaches that there are potentially postive and negative effects from tibolone (See, e.g. Haeggni at page 649, last paragraph). Berglund as cited in the Office Action does not teach balancing of risk factors nor does it remedy the acknowledged deficiency of Haenggi et al. (no teaching that tibolone inhibits atherolsclerosis).

Furthermore, the non-obviousness of the currently claimed invention is made clear by the date presented in Table III of the application and discussed in the last paragraph of I. above.

CONCLUSION

For all the foregoing reasons, it is respectfully submitted that the rejection over Haenggi et al alone and in combination with Berglund should be traversed.

Fee Authorization

Authorization for charging applicants deposit account for the Appeal Brief and Petition for Extension of Time can be found on the accompanying Transmittal letter.

Respectfully submitted,

Dated: December 7, 2005

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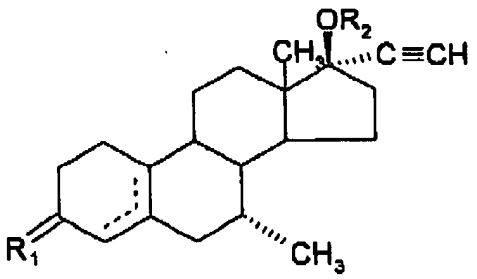
CLAIMS APPENDIX

1. (Previously presented) A method of inhibiting the atherosclerotic process, comprising administering to a mammal suffering from atherosclerosis an effective amount of a 7α-methyl-17α-ethynyl-estrane derivative having the general formula I



Formula I

wherein

R_1 = H(OR_3) or O;

R_2 = H or (C_{1-18})Acyl;

R_3 = H or (C_{1-18})Acyl;

and the dotted line represents a double bond in the 4, 5- or the 5, 10-position.

2. (Previously presented) The method according to claim 1, wherein R_1 = (H, OH) or O.

3. (Original) The method according to claim 1 or 2, wherein R_2 = H and the dotted line represents a double bond in the 5, 10-position.

4. (Original) The method according to claim 1, wherein the a 7α-methyl-17α-ethynyl-estrane derivative is 7α-methyl-17α-ethynyl-17β-hydroxy-estra-5(10)-en-3-one.

5. (Cancelled)

6. (Presently Amended) The method of Claim 1 ~~5~~ wherein the mammal is a human.

EVIDENCE APPENDIX

Not Applicable

RELATED PROCEEDINGS APPENDIX

Not Applicable.